Different forms of the neural cell adhesion molecule (NCAM).

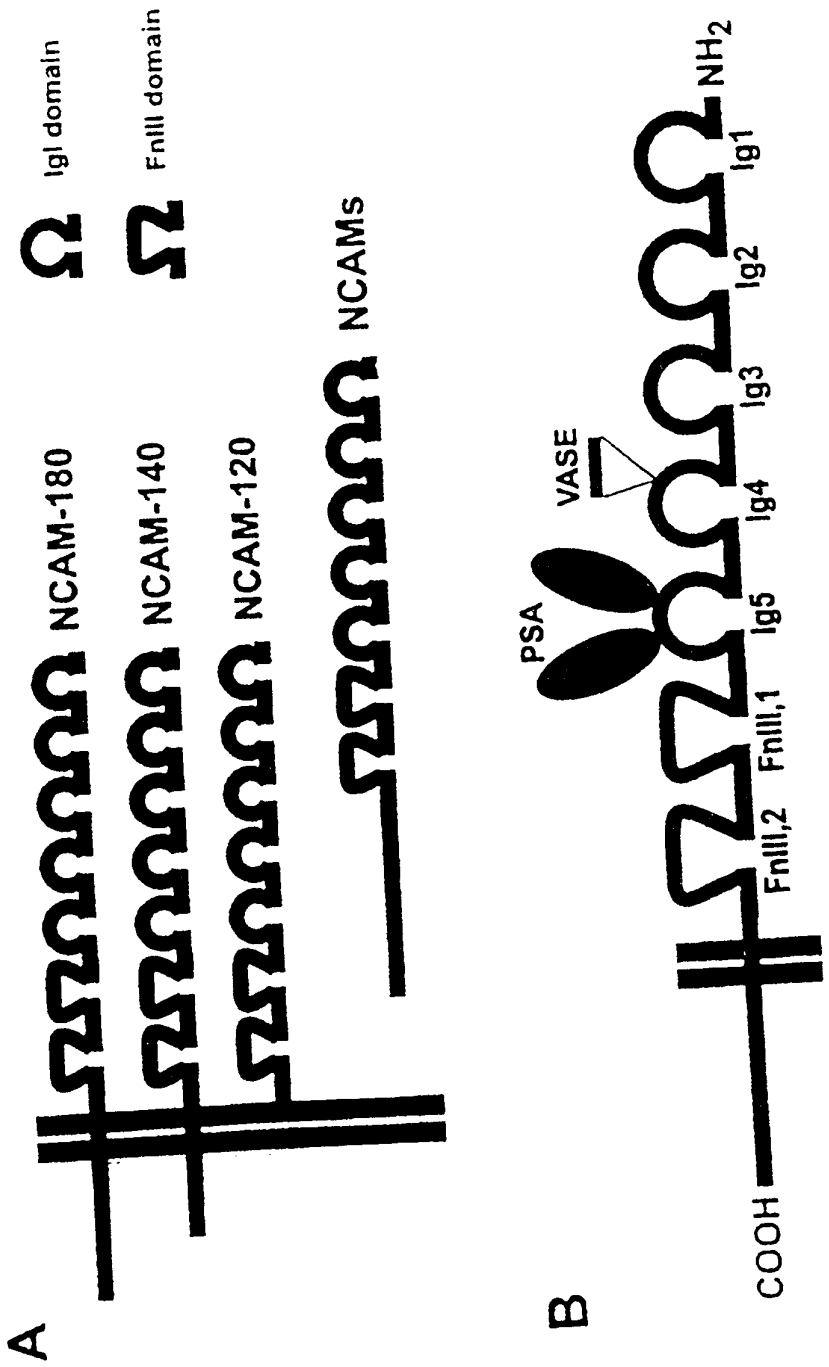
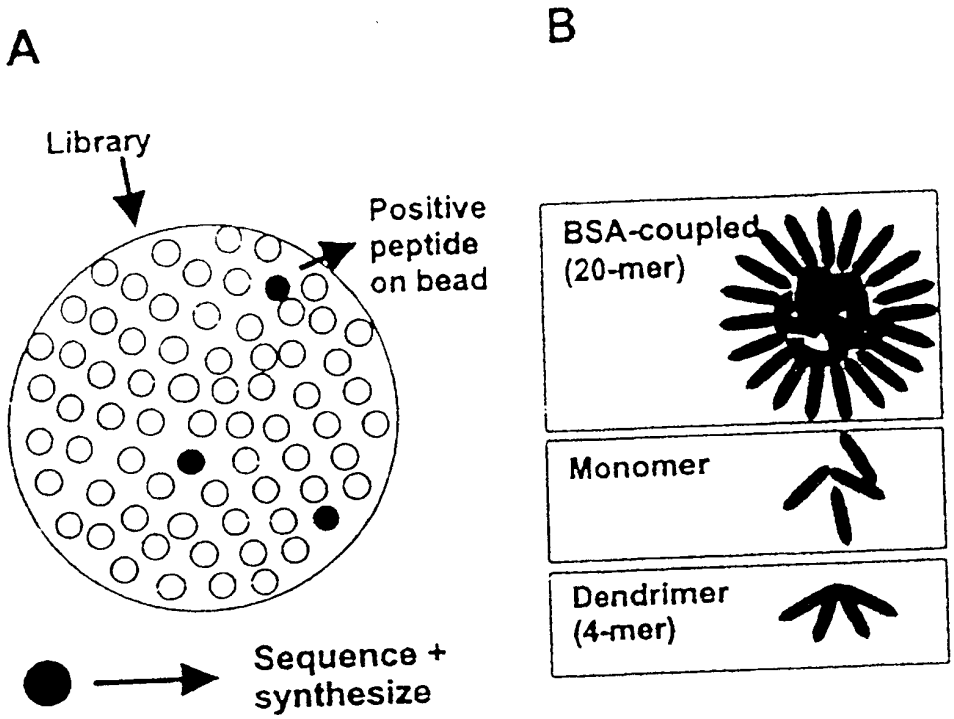


FIG. 1

Identification of synthetic peptide ligands of the NCAM Ig1 domain by means of combinatorial peptide-libraries.



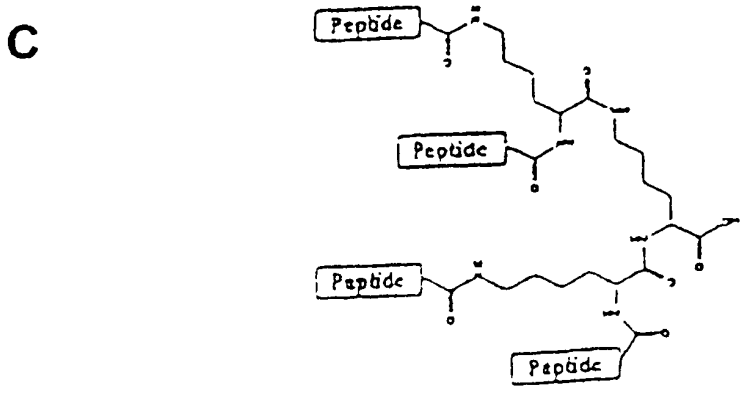


FIG. 2

Stimulation of neurite outgrowth by the C3-peptide.

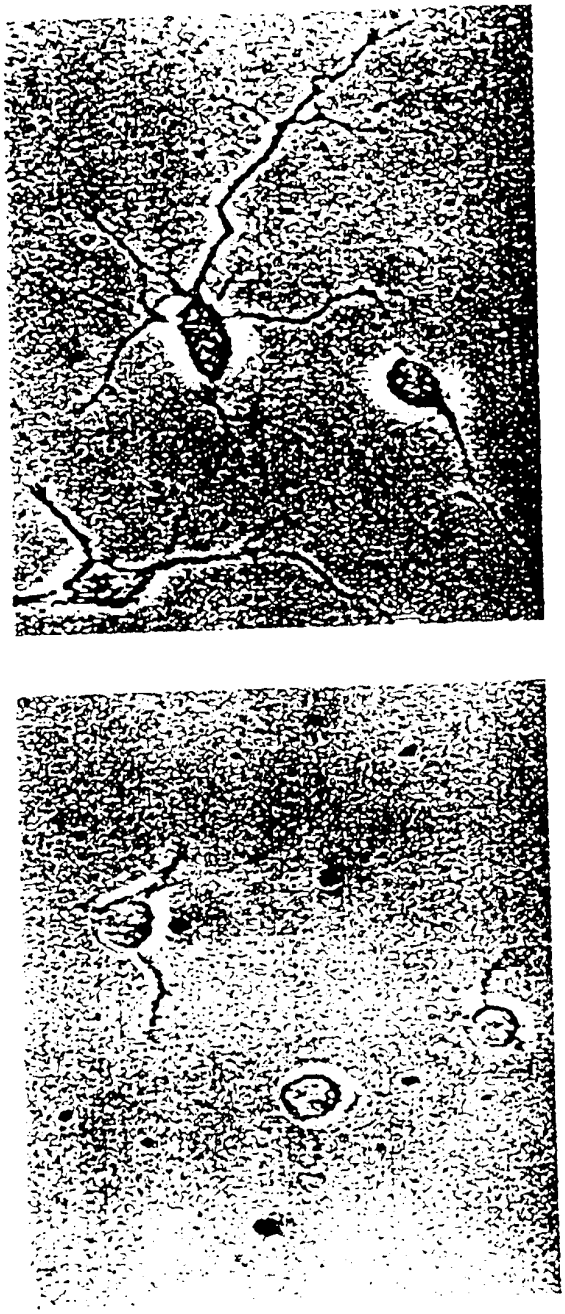


FIG. 3

NCAM-Ig1 binding sequences identified from a combinatorial library of synthetic peptides.

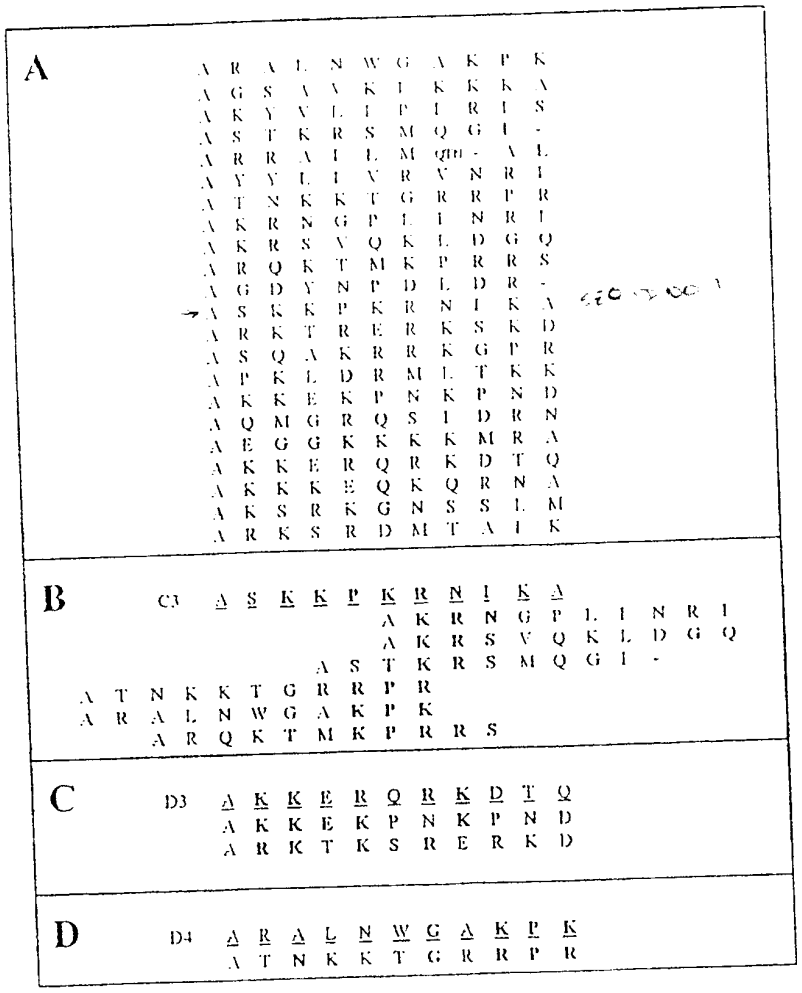
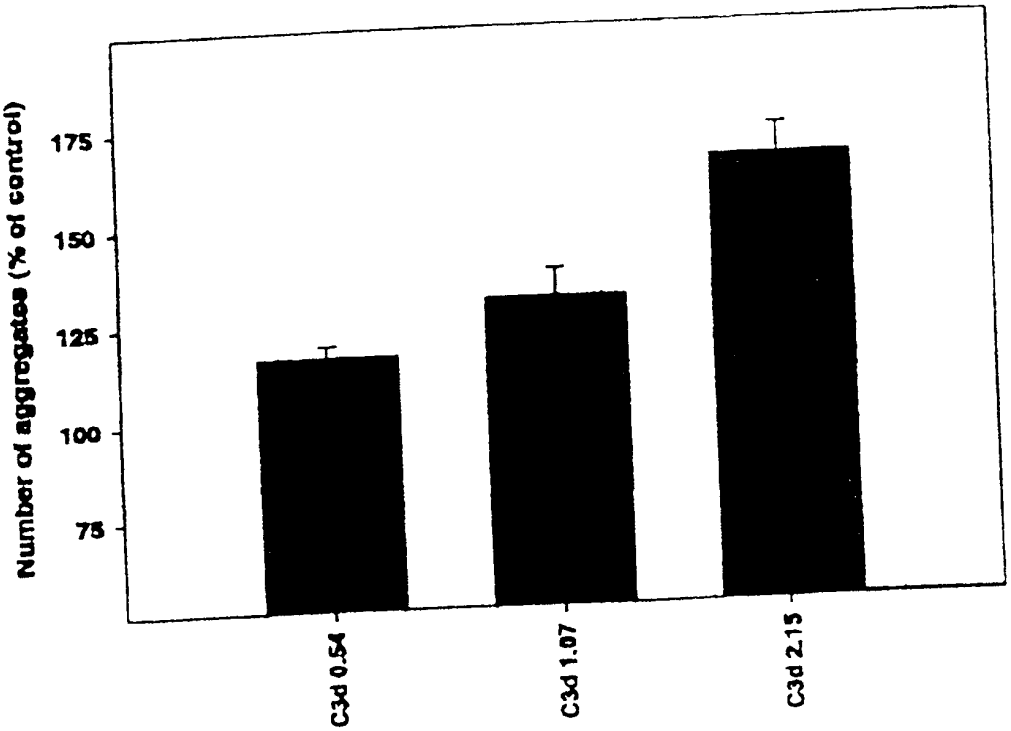


FIG. 4

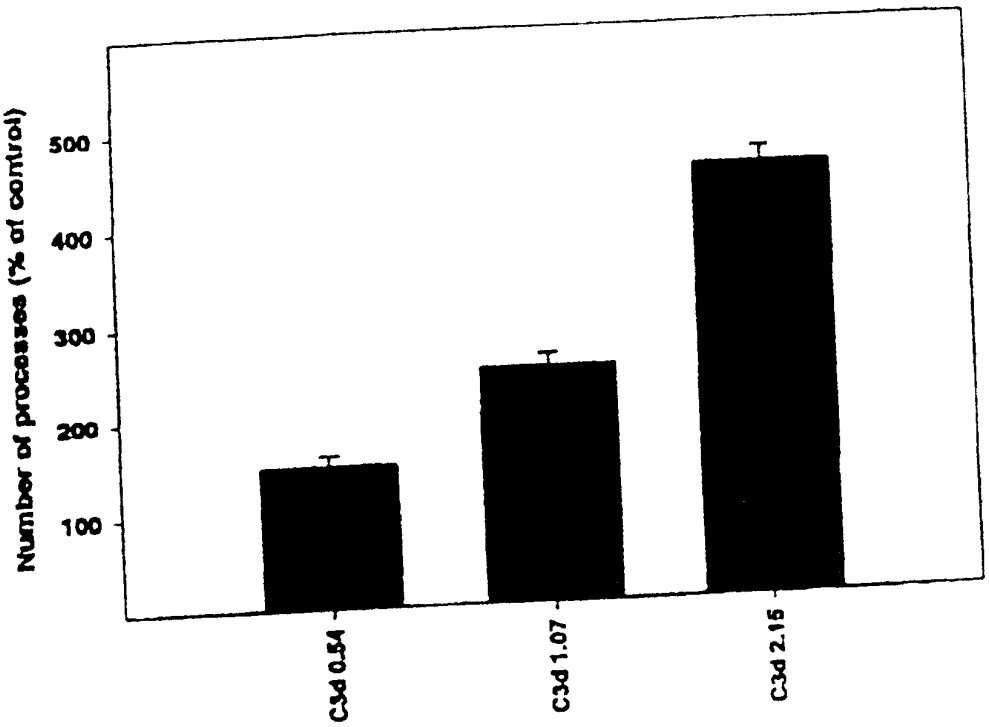
Inhibition of cell aggregation by the C3-peptide.

FIG. 5



C3-peptide promotes the formation of neuronal processes in primary cell cultures.

FIG. 6



Effect of NCAM-Ig1 binding peptides on cell aggregation and neurite outgrowth.

Controls for NCAM Ig1 binding peptide (C3)

Peptide	Sequence												Effect*	
													Neur	agg
C3	A	S	K	K	P	K	R	N	I	K	A	A	++	-
C3diacetyl. K (120)	A	S	K#	K#	P	K#	R	N	I	K#	A	A	+	-
Ala subst K/R														
116	A	S	K	K	P	K	A	N	I	K	A	A	0	0
117	A	S	K	K	P	A	A	N	I	K	A	A	0	0
118	A	S	K	A	P	A	A	N	I	K	A	A	0	0
119	A	S	A	A	P	A	A	N	I	K	A	A	++	+
P->A	A	S	K	K	A	K	R	N	I	K	A	P	++	+
122	A	S	K	K	A	K	A	N	I	K	A	K	++	+
Scrambled C3	A	K	K	K	K	R	I	S	A	K	K	A	++	+
121	P	N	A	S	I	R	K	K	K	A	K	K	++	+
114	K	N	S	P	K	A	R	I	D	T	Q	K	++	+
C3scr	A	K	K	E	R	Q	R	K	E	R	K	K	++	+
D3	R	T	K	Q	D	K	A	Q	K	P	K	A	++	+
scrabled D3	A	R	A	L	N	W	G	A	K	A	A	K	++	+
D4	G	L	K	R	W	A	P	N	K	A	K	K	+	-
Scrambled D4														
Poly-K														
K6 (dendrimer 115)	K	K	K	K	K	K	K	K	K	K	K	K	-	-

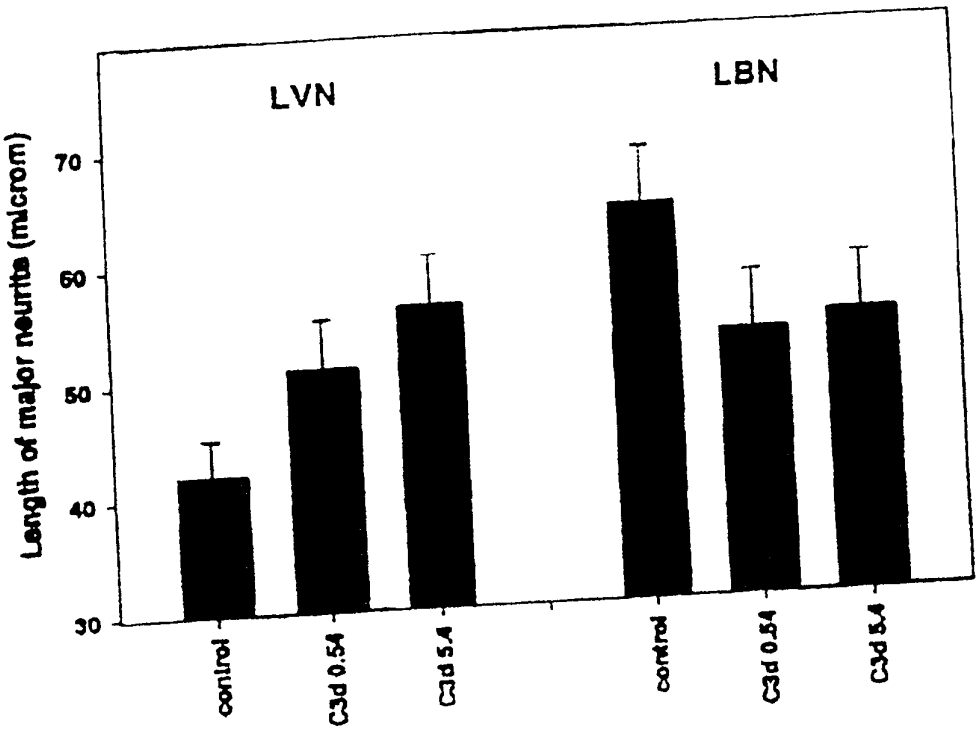
• effect on neurite extension (neur) and aggregation (agg)

acetylation on lysine

FIG. 7

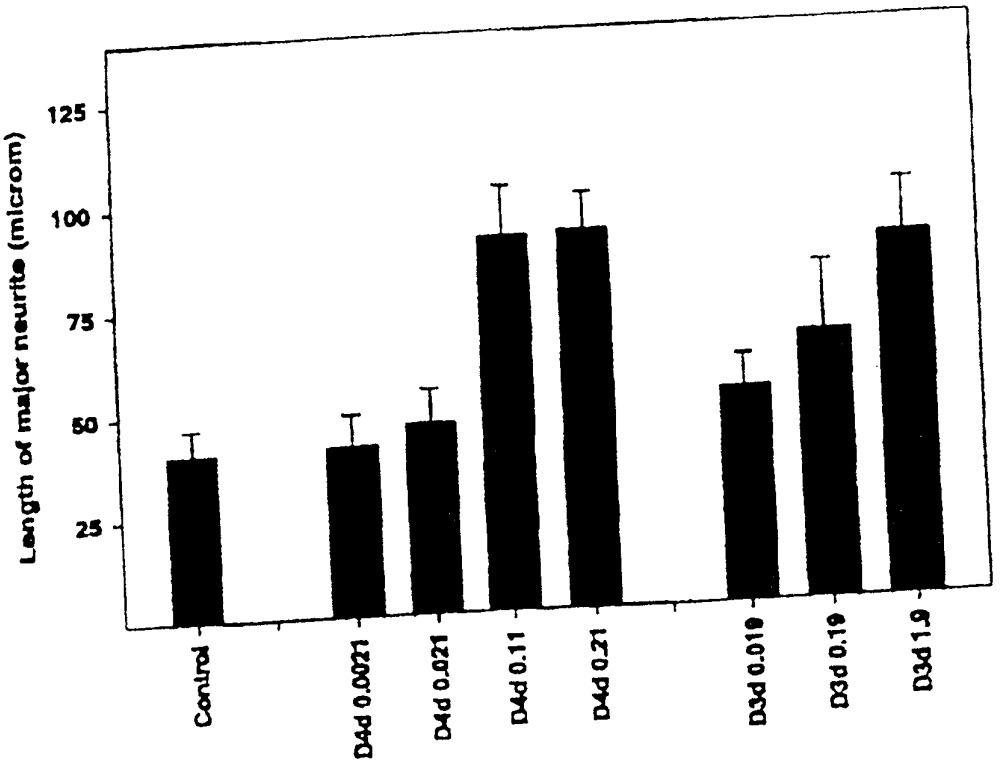
Effect of the C3-peptide on neurite outgrowth induced by NCAM-NCAM binding in cocultures of neurons and fibroblasts.

FIG. 8



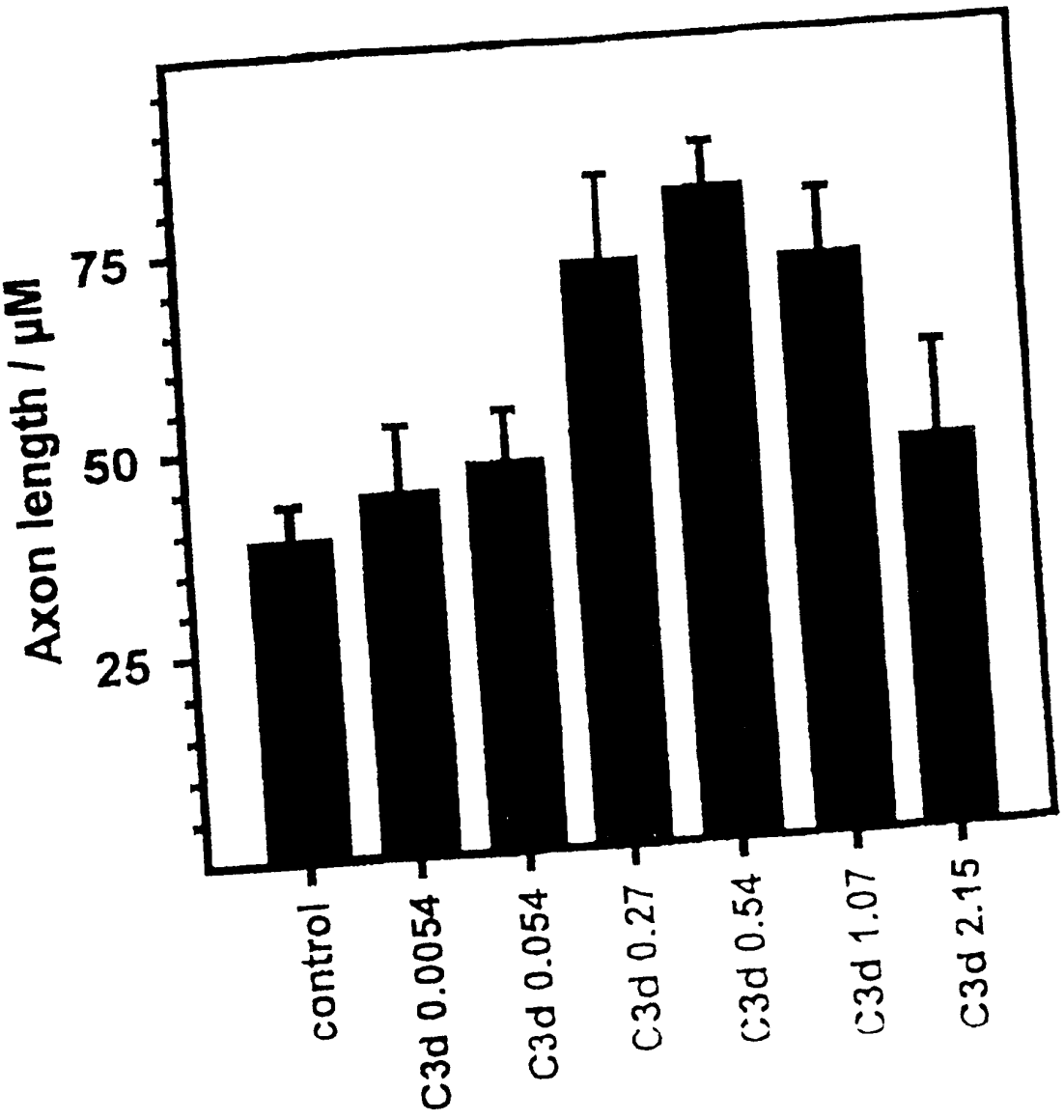
Effect of the D3- and D4-peptides on neurite outgrowth in primary hippocampal cell cultures.

FIG. 9



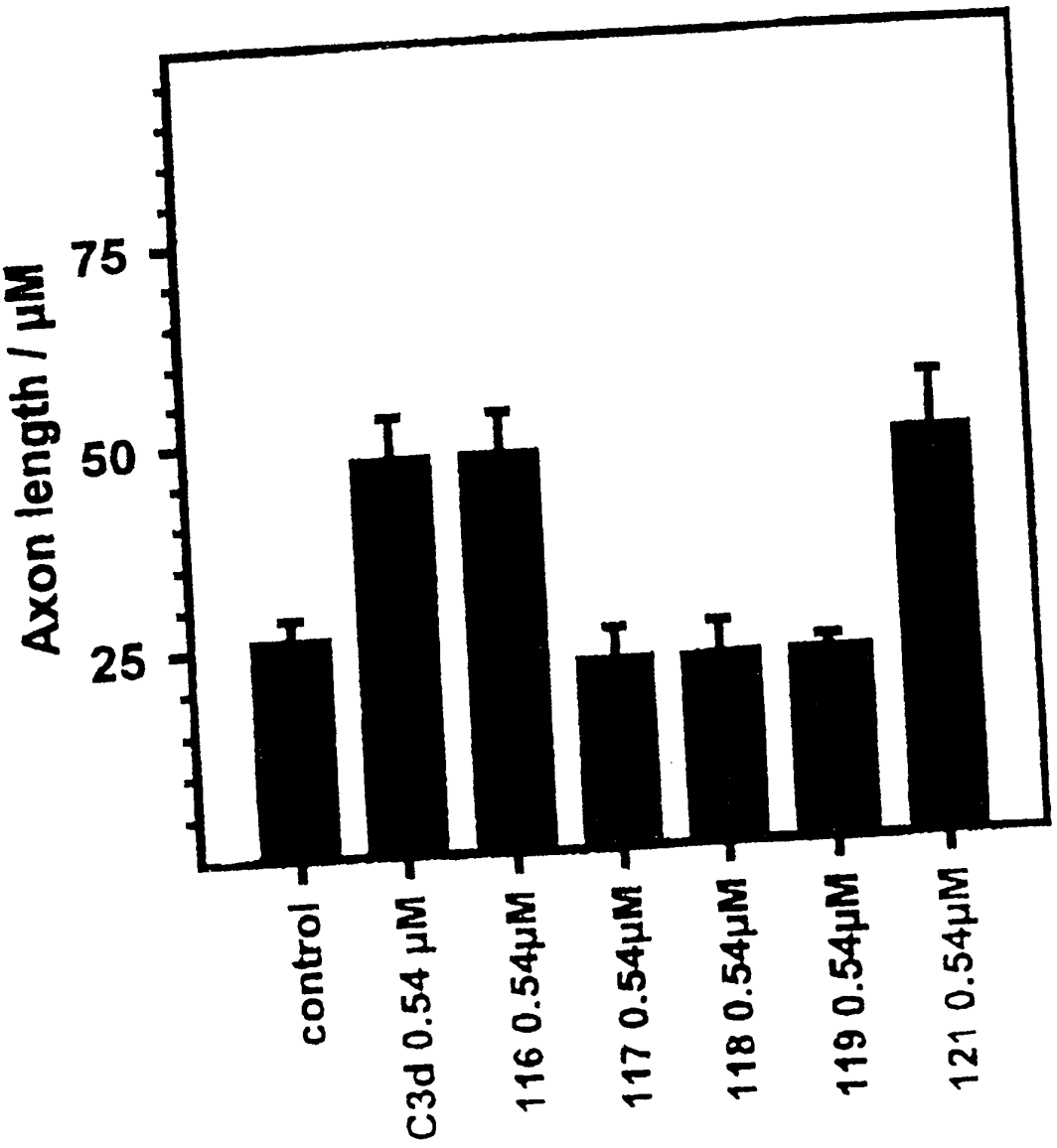
Effect of C3-peptide on neurite outgrowth.

FIG. 10



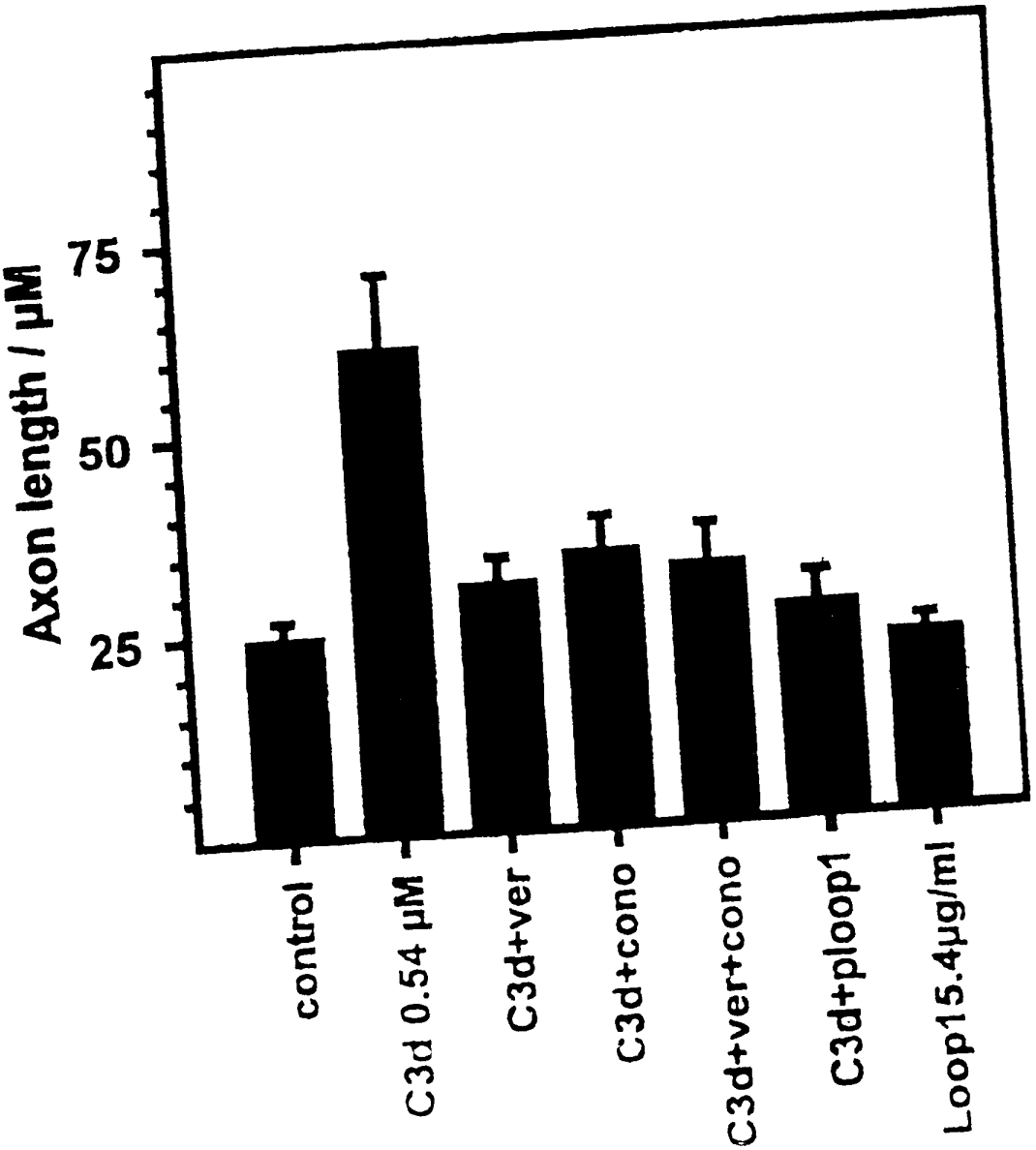
Effect of C3 and control peptides on neurite outgrowth.

FIG. 11



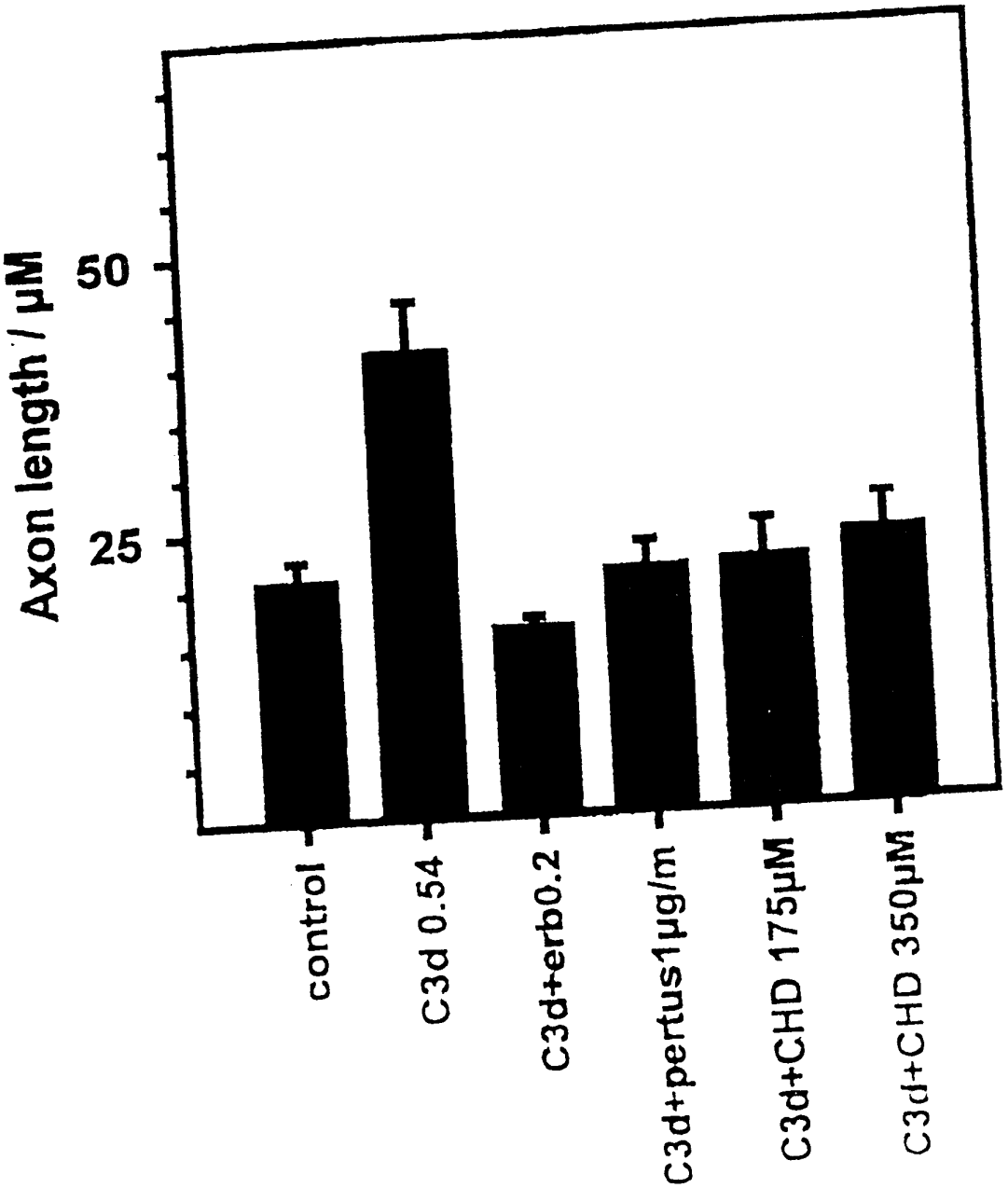
Effect of signal transduction inhibitors on C3-stimulated neurite outgrowth.

FIG. 12



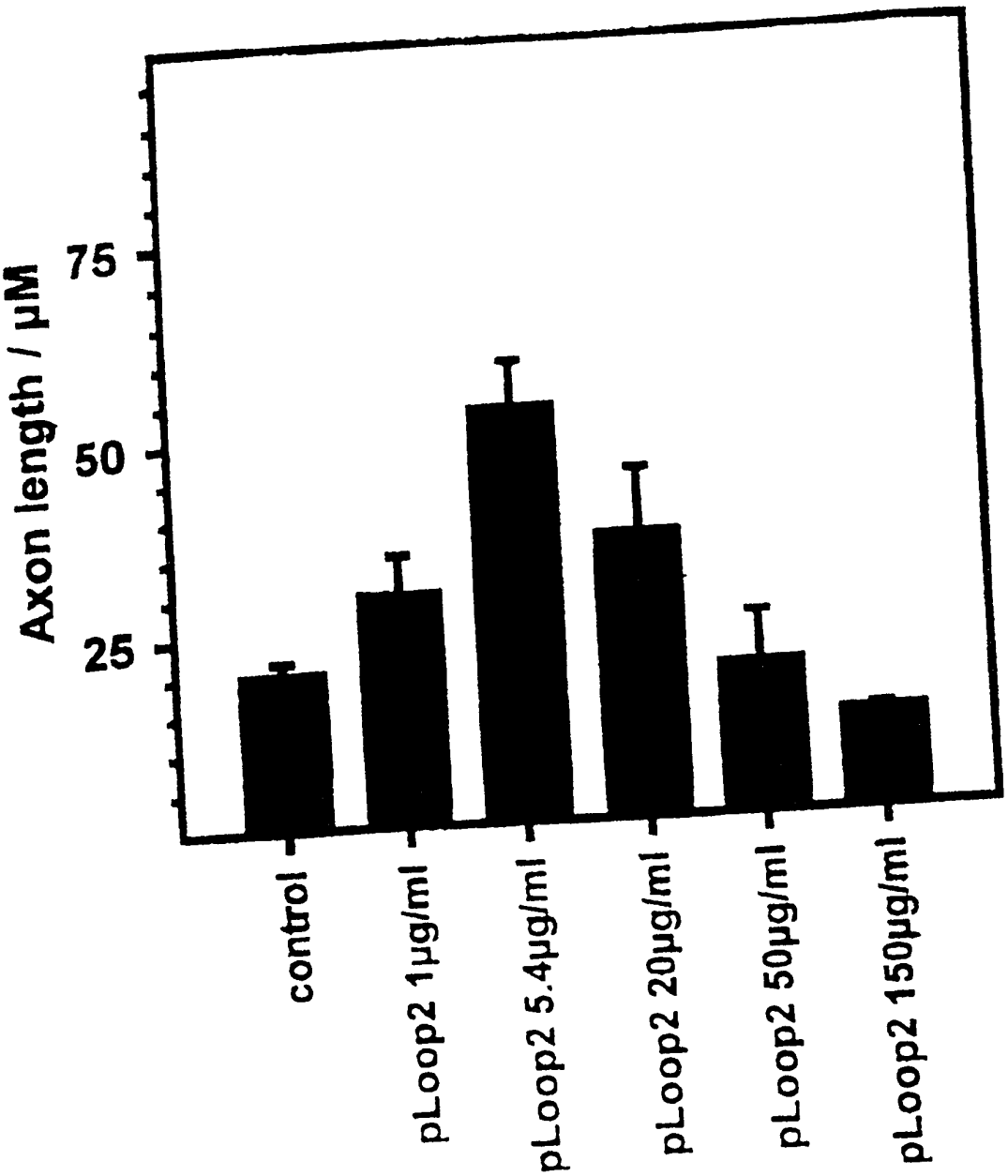
Effect of signal transduction inhibitors on C3-stimulated neurite outgrowth.

Fig. 13



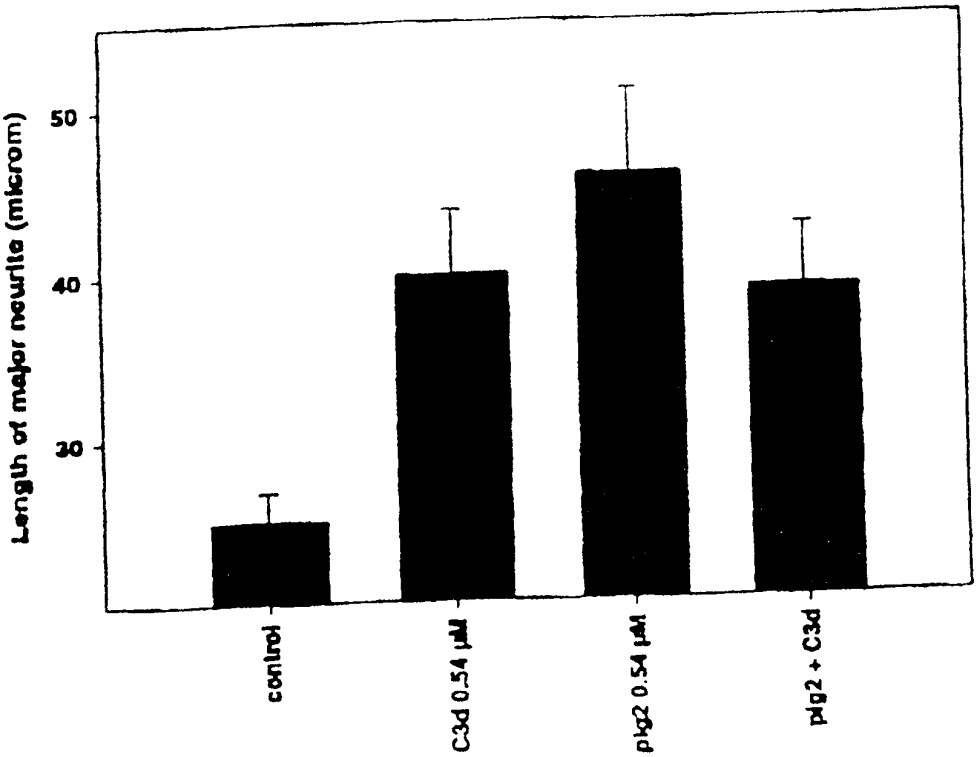
Effect of the recombinant NCAM Ig2 domain on neurite outgrowth in primary hippocampal cell cultures.

Fig. 14



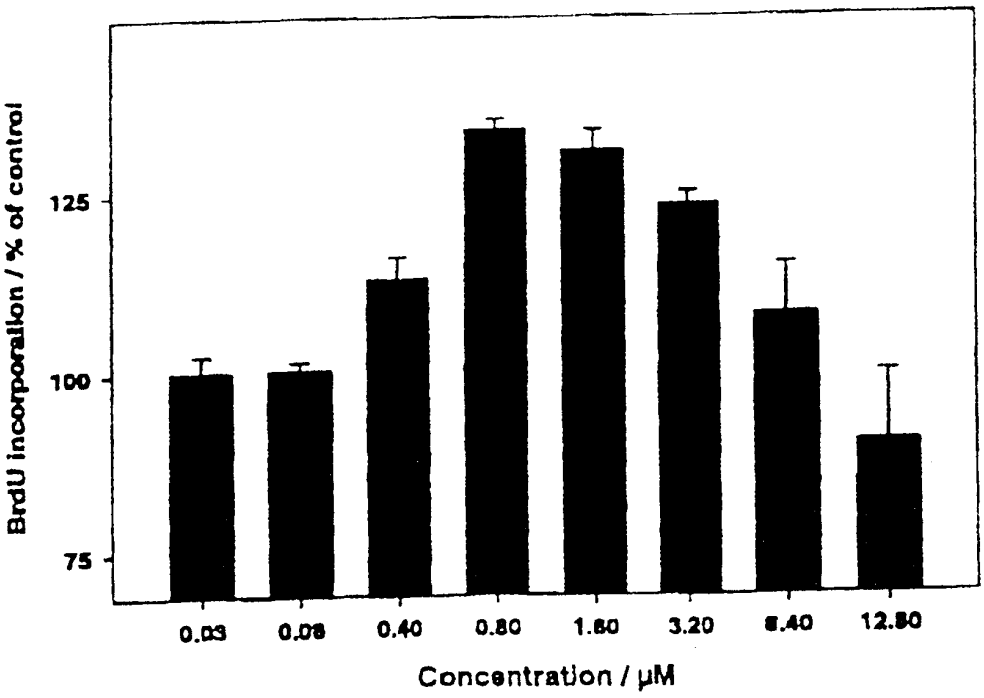
Effect of NCAM Ig2 and C3 on neurite outgrowth.

FIG. 15



Effect of the C3-peptide on proliferation of primary hippocampal cells.

FIG. 16

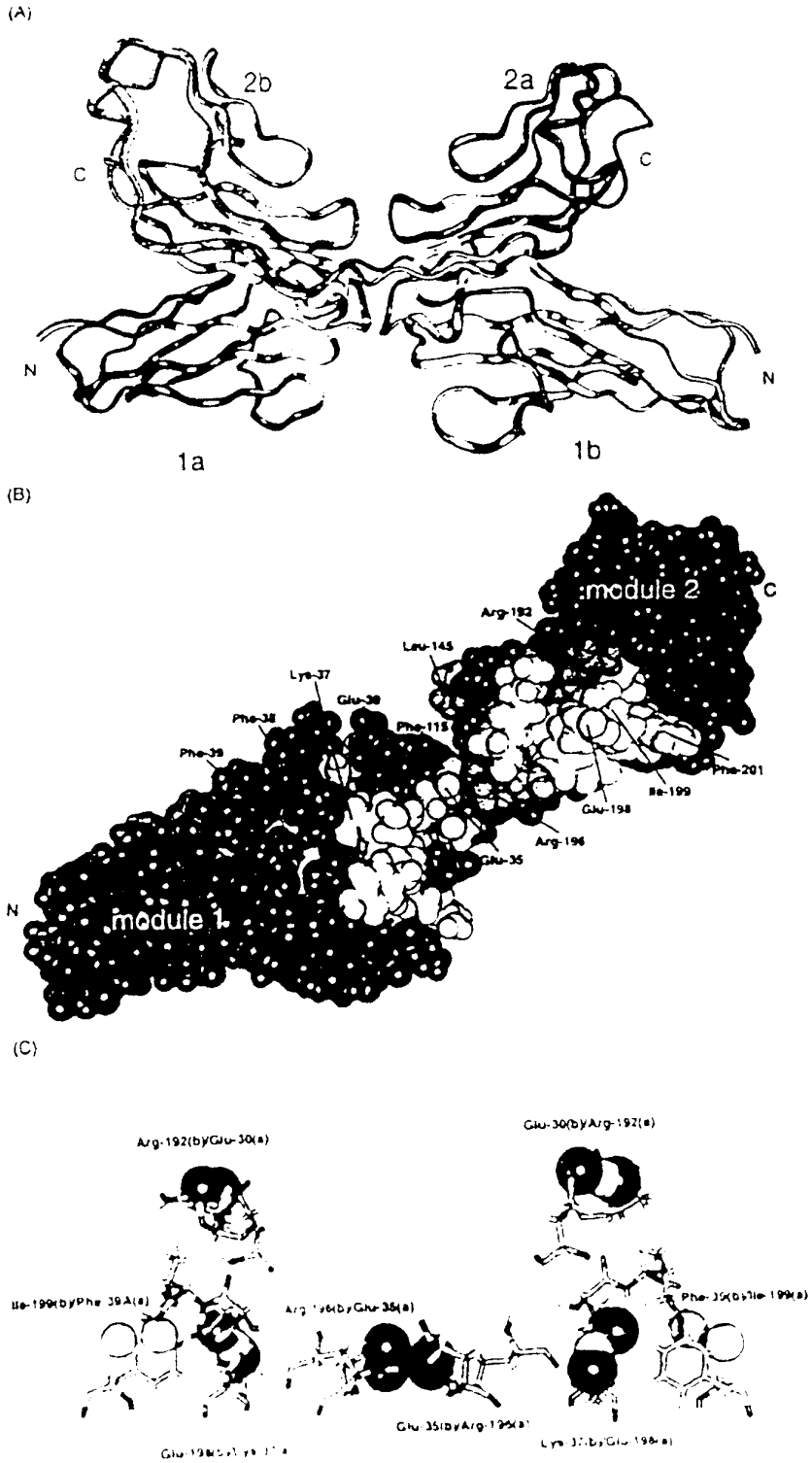


The predicted amino acid sequence of human NCAM-140.

```
  1 MLQTKDLIWT LFFLGTAVSL QVDIVPSQGE ISVGESKFFL CQVAGDAKDK DISWFSPNGE
 61 KLTPNQQRIS VVWNDDSSST LTIYNANIDD AGIYKCVVTG EDGSESEATV NVKIFQKLMF
121 KNAPTPQEFR EGEDAVIVCD VVSSLPPTII WKHKGRDVIL KKDVRFIVLS NNYLQIRGIK
181 KTDEGTYRCE GRILARGEIN FKDIQVIVNV PPTIQARQNI VNATANLGQS VTLVCDAEGF
241 PEPTMSWTKD GEQIEQEEDD EKYIFSDDSS QLTIKKVDKN DEAEYICIAE NKAGEQDATI
301 HLKVFAKPKI TYVENQTAME LEEQVTLTCE ASGDPIPSIT WRTSTRNISS EEKTLDGHMV
361 VRSHARVSSL TLKSIQYTDA GEYICTASNT IGQDSQSMYL EVQYAPKLQG PVAVYTWEGN
421 QVNITCEVFA YPSATISWFR DGQLLPSSNY SNIKIYNTPS ASYLEVTPDS ENDFGNYNCT
481 AVNRIGQESL EFILVQADTP SSPSIDQVEP YSSTAQVQFD EPEATGGVTI LKYKAEWRAV
541 GEEVWHSKWY DAKEASMEGI VTIVGLKPET TYAVRLAALN GKGLGEISAA SEFKTQPVQG
601 EPSAPKLEGQ MGEDGNSIKV NLIKQDDGGS PIRHYLVRYR ALSSEWKPEI RLPSGSDHVM
661 LKSLDWNAEY EVYVVAENQQ GKSKAAHFVF RTSAQPTAIP ANGSPTSGLS TGAIVGILIV
721 IFVLLLVVVD ITCYFLNKCG LFMCIAVNLC GKAGPGAKGK DMEEGKAAFS KDESKEPIVE
781 VRTEEERTPN HDGGKHTEPN ETTPLTEPEK GPVEAKPECQ ETETKPAPAE VKTVPNDATQ
841 TKENESKA
```

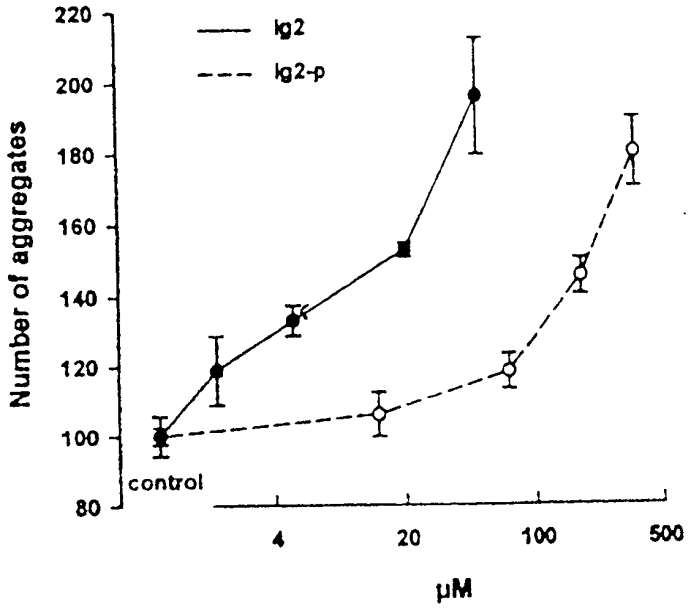
FIG. 17

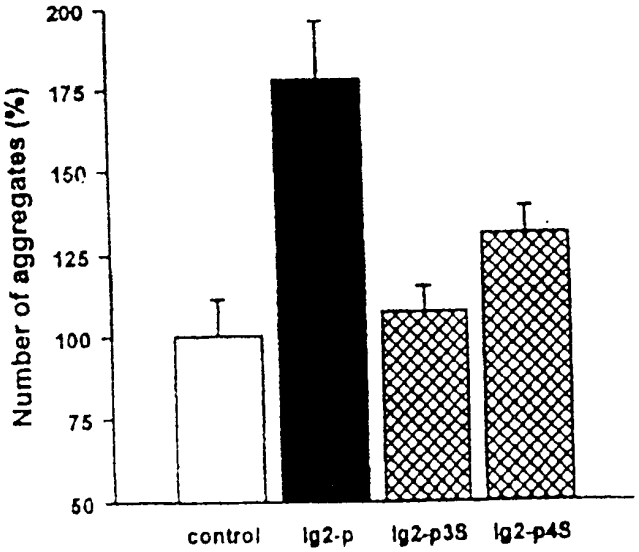
The structure of the NCAM Ig1 and Ig2 domains when binding in a dimer.



The effect of the NCAM Ig2 domain and the Ig2-p peptide and control peptides derived from the Ig2-p peptide on cell aggregation.

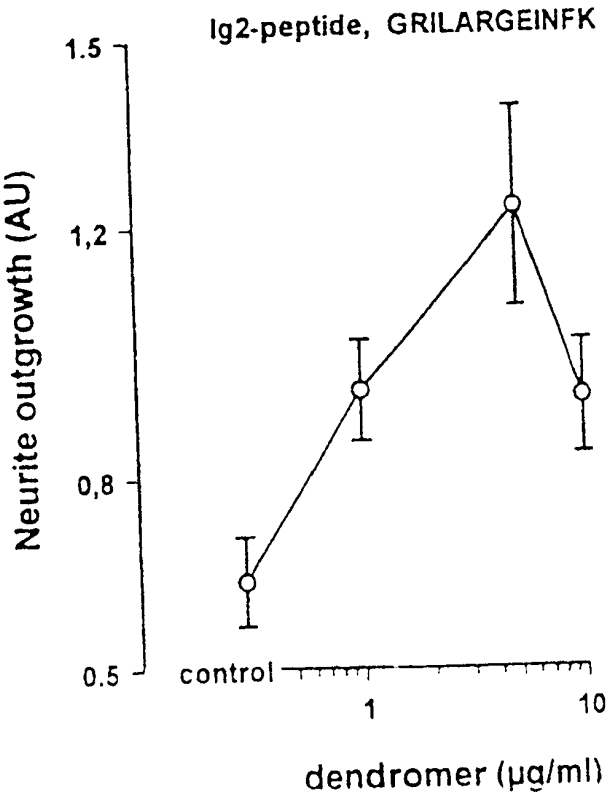
Fig. 19





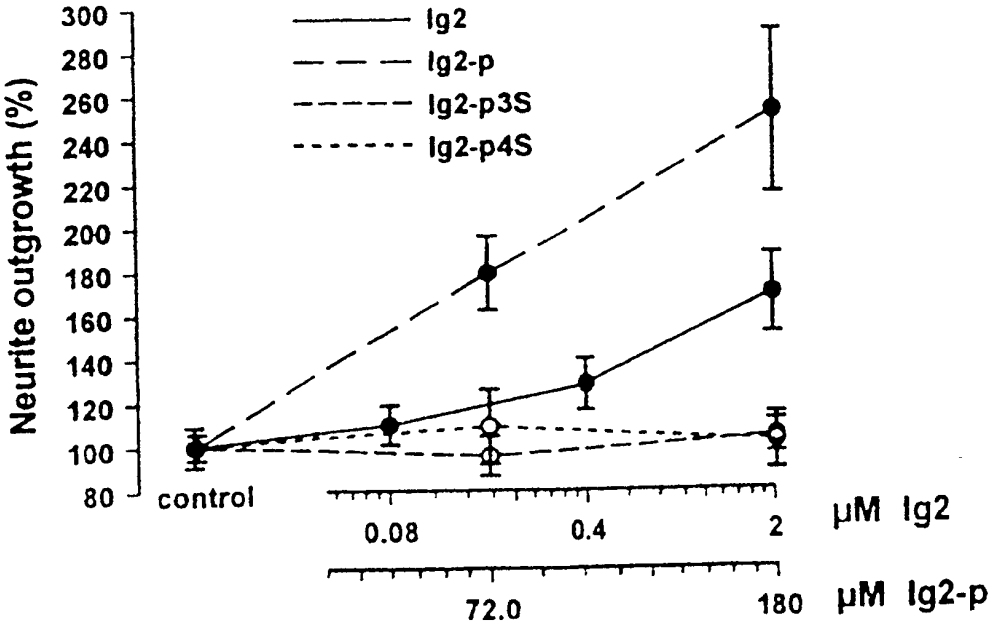
The effect of the Ig2-p peptide dendrimer on neurite outgrowth.

Fig. 20



Effect of the NCAM Ig2 domain and the Ig2-p peptide and control peptides derived from the Ig2-p peptide on neurite outgrowth.

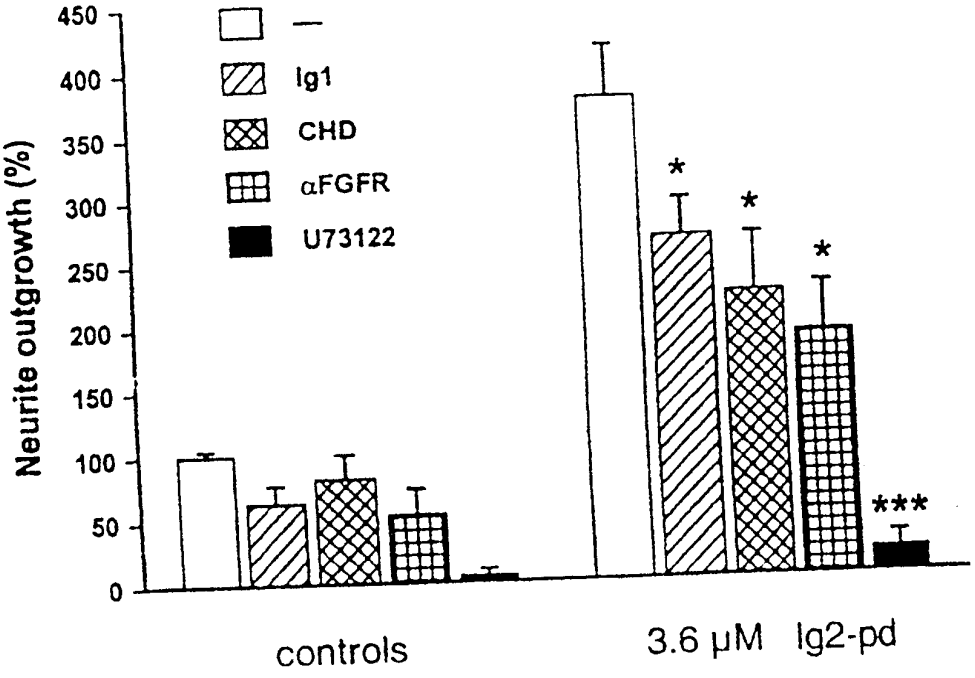
Fig. 21



Micrograph showing the effect of the Ig2-p peptide on neurite outgrowth.

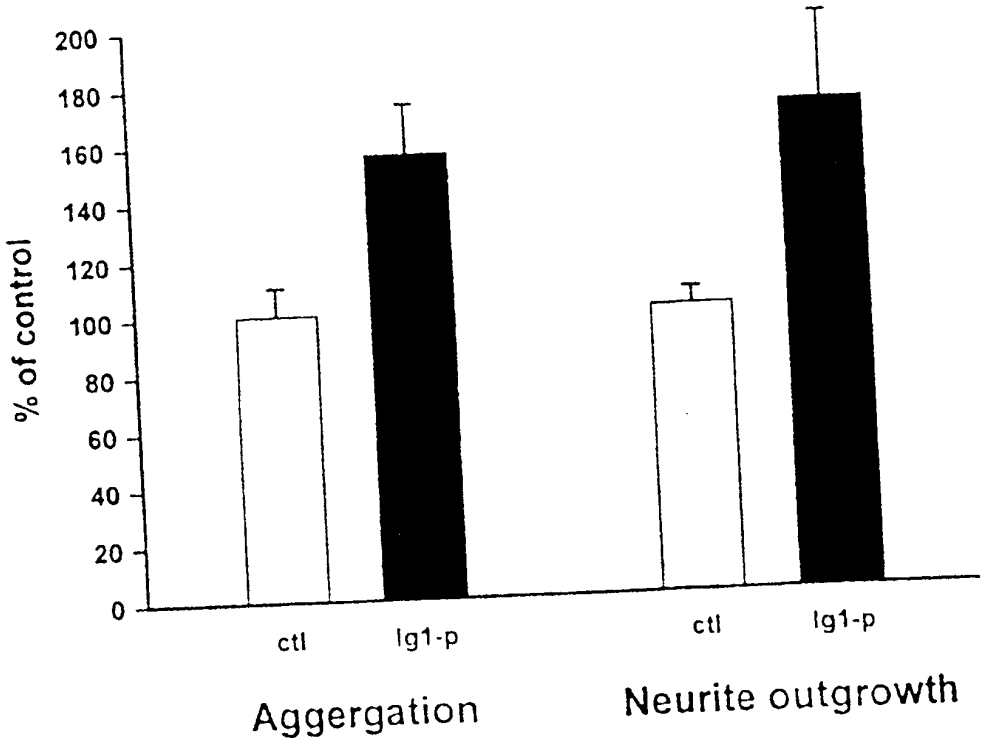
Effect of signal transduction inhibitors on neurite outgrowth stimulated by the Ig2-p peptide.

Fig. 23



Effect of the Ig1-p peptide on neurite outgrowth.

Fig. 24



Effect of mutations in the combined NCAM Ig1-Ig2 domain on neurite outgrowth.

Fig. 25